

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

Claims 1-3. (Canceled)

Claim 4. (Original): A pharmaceutical composition for use in treating progressive dementia or brain degeneration,  $\beta$ -amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities comprising a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof together with one or more pharmaceutically acceptable diluents or carriers therefore.

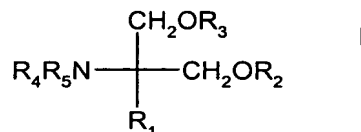
Claim 5. (Original): A pharmaceutical combination comprising a) a first agent which is a S1P receptor agonist or a pharmaceutically acceptable salt thereof and b) a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia.

Claim 6. (Original): A combination according to claim 5, wherein co-agent b) is selected from an AMPA receptor agonist, a nootropic or anti-inflammatory agent or a painkiller.

Claim 7. (Original): A method for treating progressive dementia or brain degeneration or  $\beta$ -amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof.

Claim 8. (Original): A method according to claim 7 comprising co-administration, e.g. concomitantly or in sequence, of b) a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia.

Claim 9. (Currently amended): A ~~method, composition, combination or use~~ according to ~~any one of the preceding claims~~ 4, wherein the S1P receptor agonist is compound of formula I



wherein R<sub>1</sub> is straight- or branched (C<sub>12-22</sub>)carbon chain

- which may have in the chain a bond or a hetero atom selected from a double bond, a triple bond, O, S, NR<sub>6</sub>, wherein R<sub>6</sub> is H, alkyl, aralkyl, acyl or alkoxycarbonyl, and carbonyl, and/or

- which may have as a substituent alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, acyl, alkylamino, alkylthio, acylamino, alkoxycarbonyl, alkoxycarbonylamino, acyloxy, alkylcarbamoyl, nitro, halogen, amino, hydroxyimino, hydroxyl or carboxy; or

R<sub>1</sub> is

- a phenylalkyl wherein alkyl is a straight- or branched (C<sub>6-20</sub>)carbon chain; or
- a phenylalkyl wherein alkyl is a straight- or branched (C<sub>1-30</sub>)carbon chain wherein said phenylalkyl is substituted by
- a straight- or branched (C<sub>6-20</sub>)carbon chain optionally substituted by halogen,
- a straight- or branched (C<sub>6-20</sub>)alkoxy chain optionally substituted by halogen,
- a straight- or branched (C<sub>6-20</sub>)alkenyloxy,
- phenylalkoxy, halophenylalkoxy, phenylalkoxyalkyl, phenoxyalkoxy or phenoxyalkyl,
- cycloalkylalkyl substituted by C<sub>6-20</sub>alkyl,
- heteroarylalkyl substituted by C<sub>6-20</sub>alkyl,
- heterocyclic C<sub>6-20</sub>alkyl or
- heterocyclic alkyl substituted by C<sub>6-20</sub>alkyl,

and wherein

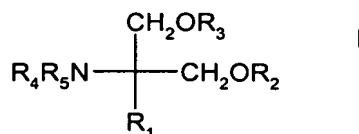
the alkyl moiety may have

- in the carbon chain, a bond or a heteroatom selected from a double bond, a triple bond, O, S, sulfinyl, sulfonyl, or NR<sub>6</sub>, wherein R<sub>6</sub> is as defined above, and
- as a substituent alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, acyl, alkylamino, alkylthio, acylamino, alkoxycarbonyl, alkoxycarbonylamino, acyloxy, alkylcarbamoyl, nitro, halogen, amino, hydroxyl or carboxy, and

each of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub>, independently, is H, C<sub>1-4</sub>alkyl or acyl or a pharmaceutically acceptable salt thereof.

Claim 10. (Currently amended): A ~~method, composition, combination or use~~ according to claim 9, wherein the S1P receptor agonist is 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol in free form or in a pharmaceutically acceptable salt form.

Claim 11. (New): A combination according to claim 5, wherein the S1P receptor agonist is compound of formula I



wherein R<sub>1</sub> is straight- or branched (C<sub>12-22</sub>)carbon chain

- which may have in the chain a bond or a hetero atom selected from a double bond, a triple bond, O, S, NR<sub>6</sub>, wherein R<sub>6</sub> is H, alkyl, aralkyl, acyl or alkoxycarbonyl, and carbonyl, and/or

- which may have as a substituent alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, acyl, alkylamino, alkylthio, acylamino, alkoxycarbonyl, alkoxycarbonylamino, acyloxy, alkylcarbamoyl, nitro, halogen, amino, hydroxyimino, hydroxyl or carboxy; or

R<sub>1</sub> is

- a phenylalkyl wherein alkyl is a straight- or branched (C<sub>6-20</sub>)carbon chain; or
- a phenylalkyl wherein alkyl is a straight- or branched (C<sub>1-30</sub>)carbon chain wherein said phenylalkyl is substituted by
- a straight- or branched (C<sub>6-20</sub>)carbon chain optionally substituted by halogen,
- a straight- or branched (C<sub>6-20</sub>)alkoxy chain optionally substituted by halogen,
- a straight- or branched (C<sub>6-20</sub>)alkenyloxy,
- phenylalkoxy, halophenylalkoxy, phenylalkoxyalkyl, phenoxyalkoxy or phenoxyalkyl,
- cycloalkylalkyl substituted by C<sub>6-20</sub>alkyl,
- heteroarylalkyl substituted by C<sub>6-20</sub>alkyl,
- heterocyclic C<sub>6-20</sub>alkyl or
- heterocyclic alkyl substituted by C<sub>6-20</sub>alkyl,

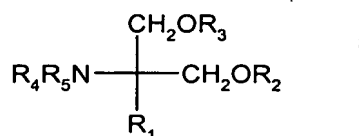
and wherein

the alkyl moiety may have

- in the carbon chain, a bond or a heteroatom selected from a double bond, a triple bond, O, S, sulfinyl, sulfonyl, or NR<sub>6</sub>, wherein R<sub>6</sub> is as defined above, and
- as a substituent alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, acyl, alkylamino, alkylthio, acylamino, alkoxycarbonyl, alkoxycarbonylamino, acyloxy, alkylcarbamoyl, nitro, halogen, amino, hydroxyl or carboxy, and

each of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub>, independently, is H, C<sub>1-4</sub>alkyl or acyl or a pharmaceutically acceptable salt thereof.

Claim 12. (New): A method according to claim 7, wherein the S1P receptor agonist is compound of formula I



wherein R<sub>1</sub> is straight- or branched (C<sub>12-22</sub>)carbon chain

- which may have in the chain a bond or a hetero atom selected from a double bond, a triple bond, O, S, NR<sub>6</sub>, wherein R<sub>6</sub> is H, alkyl, aralkyl, acyl or alkoxycarbonyl, and carbonyl, and/or
- which may have as a substituent alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, acyl, alkylamino, alkylthio, acylamino, alkoxycarbonyl, alkoxycarbonylamino, acyloxy, alkylcarbamoyl, nitro, halogen, amino, hydroxyimino, hydroxyl or carboxy; or

R<sub>1</sub> is

- a phenylalkyl wherein alkyl is a straight- or branched (C<sub>6-20</sub>)carbon chain; or

- a phenylalkyl wherein alkyl is a straight- or branched (C<sub>1-30</sub>)carbon chain wherein said phenylalkyl is substituted by
- a straight- or branched (C<sub>6-20</sub>)carbon chain optionally substituted by halogen,
- a straight- or branched (C<sub>6-20</sub>)alkoxy chain optionally substituted by halogen,
- a straight- or branched (C<sub>6-20</sub>)alkenyloxy,
- phenylalkoxy, halophenylalkoxy, phenylalkoxyalkyl, phenoxyalkoxy or phenoxyalkyl,
- cycloalkylalkyl substituted by C<sub>6-20</sub>alkyl,
- heteroarylalkyl substituted by C<sub>6-20</sub>alkyl,
- heterocyclic C<sub>6-20</sub>alkyl or
- heterocyclic alkyl substituted by C<sub>6-20</sub>alkyl,

and wherein

the alkyl moiety may have

- in the carbon chain, a bond or a heteroatom selected from a double bond, a triple bond, O, S, sulfinyl, sulfonyl, or NR<sub>6</sub>, wherein R<sub>6</sub> is as defined above, and
- as a substituent alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, acyl, alkylamino, alkylthio, acylamino, alkoxycarbonyl, alkoxycarbonylamino, acyloxy, alkylcarbamoyl, nitro, halogen, amino, hydroxyl or carboxy, and

each of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub>, independently, is H, C<sub>1-4</sub>alkyl or acyl

or a pharmaceutically acceptable salt thereof.

Claim 13. (New): A combination according to claim 11, wherein the S1P receptor agonist is 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol in free form or in a pharmaceutically acceptable salt form.

Claim 14. (New): A method according to claim 12, wherein the S1P receptor agonist is 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol in free form or in a pharmaceutically acceptable salt form.